Highly Enantioselective Alkynylation of α-Keto Ester: An Efficient Method for Constructing a Chiral Tertiary Carbon Center

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Melting point were uncorrected. ^{1}H NMR spectra were recorded on 300 MHz spectrometers with TMS as an internal standard and $CDCl_3$ as solvent. ^{13}C NMR spectra were recorded on 75 MHz spectrometers with TMS as an internal standard and $CDCl_3$ as solvent. ^{19}FNMR spectra were recorded on 282 MHz spectrometer with $CDCl_3$ as solvent. Coupling constants, *J* values, were given in Hz. IR spectra were taken on a Shimadzu 440-IR spectrophotometer. MS spectra were run respectively on a finnigan 4021 GC MS/DC and Varian MAT 21 instrument with an ionizing voltage of 70eV.

Preparation of (1*S*,2*S*)-2-*N*,*N*-dimethylamino-3-(*p*-nitrophenyl)propane- 1,3-diol: (1*S*,2*S*)-2-amino-3-(*p*-nitrophenyl)propane-1,3-diol **(1)** (5 g, 23.6 mmol), aqueous HCHO (37-40%, 7.5 mL) and HCOOH (98%, 10 mL) was added to a 25 mL flask and refluxed for 8 h. After removal of the solvent under reduced pressure, the residue was neutralized with 1N NaOH (30 mL) and extracted with CH_2Cl_2 (3 x 30 mL). The combined organic phase was washed with brine, dried (Na_2SO_4) and filtered. After removed of the solvent, the residue was subjected to flash chromatography on a short basic Al_2O_3 column (eluted with CH_2Cl_2 /CH_3OH=10:1) to give product (5.6 g, 99%) as a brown solid: mp 88.8-89.1 ^{o}C; $[\alpha]_D^{20}$= + 25.7 (*c*, 0.505, CH_3OH); ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 8.20 (d, *J* = 7.8 Hz, 2H), 7.58 (d, *J* = 7.8 Hz, 2H), 4.55 (d, *J* = 9.6 Hz, 1H), 3.60 (d, *J* = 4.5 Hz, 2H), 2.60-2.55

(m, 1H), 2.53 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C 150.0, 147.0, 127.7, 123.2, 70.8, 69.6, 57.1, 41.2 ppm; IR (neat) 3366, 3069, 2980, 2918, 1694, 1599, 1525, 1352, 1199, 1061, 998, 858, 832, 748, 698; Ms *m/e* (relative intensity) 240 (M^+, 8.15), 200 (2.90), 195 (7.07), 153 (5.34), 105 (21.56), 88 (85.87), 58 (48.55), 42 (100.00); Anal. calcd. for $C_{11}H_{16}N_2O_4$: C, 54.99; H, 6.71; N, 11.66. found: C, 54.92; H, 6.81%; N, 11.35.

Preparation of (1*S*,2*S*)-3-(*t*-butyldimethylsilyloxy)-2-*N*,*N*-dimethylamino–1-(*p*-nitro phenyl)propane-1-ol (1):

A solution of above substrate (1.95 g, 8.1 mmol) in CH_2Cl_2 (30 mL) was treated with *tert*-butyldimethysilylchloride (1.28 g, 8.5 mmol), imidazole (1.4 g, 20.6 mmol) and a catalytic amount of DMAP (10 mg) overnight at rt under N_2. The reaction mixture was poured into water (20 mL) and then neutralized with cold aqueous HCl (0.5 M) to pH=8. The aqueous phase was extracted with CH_2Cl_2 (2 x 10 mL). The combined organic phase was washed with saturated Na_2CO_3 solution, brine, dried with anhydrous Na_2SO_4 and filtered. After removal of solvent, the residue was purified by flash chromatography on silica gel column (eluted with CH_2Cl_2 /CH_3OH = 20:1) to give **1** (2.72 g, 95%) as a brown oil: $[\alpha]_D^{20}$= - 15.8 (*c*, 1.09, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ_H 8.25-8.20 (d, *J* = 8.5 Hz, 2H), 7.60-7.55 (d, *J* = 8.5 Hz, 2H), 4.65 (d, *J* = 9.7 Hz, 1H), 3.7-3.6 (dd, *J* = 11.3 Hz, 2.7Hz, 1H), 3.5-3.45 (dd, *J* = 11.3 Hz, 6 Hz, 1H), 2.5 (m, 7H), 1.85 (s, 9H), 0.1 (s, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ_H 150.2, 147.4, 128.0, 123.3, 71.3, 69.0, 57.1, 41.6, 25.7, 17.9, -5.9 ppm; IR (neat) 3344, 2954, 2931, 2858, 1606, 1525, 1471, 1349, 1257, 1114, 1039, 946, 839, 777, 699; Ms *m/e* (relative intensity) 297 (M^+-57, 0.27), 209 (8.18), 203 (17.45), 202 (100.00), 163 (2.33), 129 (1.84), 73 (27.37); Anal. calcd. for $C_{17}H_{30}N_2O_4Si$: C, 57.60%; H, 8.53%; N, 7.90%. found: C, 57.82%; H, 8.18%; N, 7.77%.

General procedure for the catalytic asymmetric alkynylation addition of α-keto ester:

To a solution of $Zn(OTf)_2$ (0.2 equiv., 0.1 mmol) and chiral ligand (1*S*,2*S*)-**1** (0.22 equiv., 0.11 mmol) in terminal acetylene (3 equiv., 1.5 mmol) was added triethylamine (0.3 equiv., 0.15 mmol) under nitrogen atmosphere at ambient temperature for 2h. Then the α-keto

ester (1 equiv., 0.5 mmol) was introduced by syringe. The reaction mixture was stirred for 2 days at 70 ^{o}C. The mixture was diluted petroleum ether (20 mL) and washed with HCl (0.5 M, 3x10 mL, keeping pH≥4). The organic phase was washed with brine, distilled water, and dried with anhydrous Na_2SO_4. After removal of solvent, the crude product was purified through a short flash chromatograph (Petroleum ether/EtOAc=7/1) to yield the corresponding hydroxyl ynyl ester. The aqueous phase was neutralized with NH_4OH to pH=8 and extracted with CH_2Cl_2 (3 x 10 mL). The combined organic phase was washed with saturated aqueous Na_2CO_3, brine and distilled water, dried with anhydrous Na_2SO_4. After removal of solvent, the ligand was recovered in 98%.

Mehtyl (+)-2-hydroxyl-2,4-diphenyl-3-yn-butyrate (4a):

$Zn(OTf)_2$ (0.2 eq.) as additive, (1*S*, 2*S*)-**1** as ligand: Isolated in 91 % yield and 89 % ee (the reaction scale: Alkyne **3a** is 1.5 mmol, the α-keto ester **2a** is 0.5 mmol) as determined by HPLC analysis (Chiralcel AD, hexane / *i*-PrOH = 97 / 3, 254 nm) t_r 24.020 (major), 32.793 (minor); $Zn(ODf)_2$(0.2 eq.) as additive, (1*S*, 2*S*)-**1** as ligand: Isolated in 83 % yield and 92 %ee (the reaction scale: Alkyne **3a** is 1.5 mmol, the α-keto ester **2a** is 0.5 mmol) as determined by HPLC analysis (Chiralcel OD, *i*-PrOH / hexane = 97/3, 254 nm) t_r 32.343 (major), 44.263 (minor); $Zn(OTf)_2$ (0.2 eq.) as additive, (+)-*N*-methylephedrine **5** as ligand: Isolated in 87 % yield and 88 %ee (the reaction scale: Alkyne **3a** is 1.5 mmol, the α-keto ester **2a** is 0.5 mmol) as determined by HPLC analysis (Chiralcel OD, *i*-PrOH / hexane = 9/1, 254 nm) t_r 32.757 (minor), 44.730 (major); $[\alpha]_D^{20}$= +19.56 (*c*, 4.04, $CHCl_3$); IR (neat) 3493, 2953, 2227, 1738, 1599, 1491, 1450, 1430, 1259, 1185, 1175, 1097, 1072, 965, 766, 695 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ_H 7.79 (m, 2H), 7.55 (m, 2H), 7.40 (m, 6H), 4.40 (s, 1H), 3.80 (s, 3H) ppm. ^{13}C NMR ($CDCl_3$, 75 Hz) δ_C 172.7, 139.5, 132.2, 129.2, 129.1, 128.7, 128.6, 126.5, 122.1, 87.2, 86.6, 73.5, 54.5 ppm; Ms *m/e* (relative intensity) 266 (M^+, 0.13), 250 (M^+-16, 8.25), 207 (100.00), 178 (7.71), 129 (65.73), 105 (24.47), 77 (18.20); HRMS for $C_{17}H_{14}O_3$: 266.0947; found: 266.0945.

Ethyl (+)-2-hydroxyl-2-sulfene-4-phenyl-3-yn-butyrate (4b):

$Zn(OTf)_2$ (0.2 eq.) as additive, (1*S*, 2*S*)-**1** as ligand: Isolated in 93 % yield and 73 % ee (the reaction scale: Alkyne **3a** is 1.5 mmol, the α-keto ester **2b** is 0.5 mmol) as determined by HPLC analysis (Chiralcel AD, hexane / *i*-PrOH = 85 / 15, 254 nm) t_r 16.09 (major), 19.30 (minor); $[\alpha]_D^{20}$= +11.08 (*c*, 3.91, $CHCl_3$); IR (neat) 3473, 2983, 2232, 1737, 1490, 1444, 1368, 1249, 1233, 1159, 1094, 1043, 855, 759, 707, 691 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ_H 7.50 (m, 2H), 7.35-7.30 (m, 5H), 6.95 (m, 1H), 4.45 (br, 1H), 4.35 (m, 2H), 1.25 (m, 3H) ppm; ^{13}C NMR ($CDCl_3$, 75 Hz) δ_C 170.9, 143.7, 131.9, 129.1, 128.3, 126.9, 126.3, 126.2, 121.6, 86.7, 85.4, 70.5, 63.9, 13.9 ppm; Ms *m/e* (relative intensity) 286 (M^+, 0.12), 213 (100.00), 184 (3.66), 129 (45.10), 111 (33.38); HRMS for $C_{16}H_{14}SO_3$: 286.0657; found: 286.0660.

Methyl (+)-2-hydroxyl-2,6-diphenyl-3-yn-hexyrate (4c):

$Zn(OTf)_2$ (0.2 eq.) as additive, (1*S*, 2*S*)-**1** as ligand: Isolated in 88 % yield and 94 % ee (the reaction scale: Alkyne **3b** is 1.5 mmol, the α-keto ester **2a** is 0.5 mmol) as determined by HPLC analysis (Chiralcel AD, hexane / *i*-PrOH = 95 / 5, 254 nm) t_r 33.58 (minor), 37.64 (major); $[\alpha]_D^{20}$= +26.65 (*c*, 4.83, $CHCl_3$); IR (neat) 3487, 3030, 2954, 2853, 2243, 1737, 1602, 1450, 1434, 1255, 1147, 1082, 1074, 932, 759, 699 cm^{-1}; ^1H NMR ($CDCl_3$) δ_H 7.60 (m, 2H), 7.35-7.20 (m, 5H), 4.18 (s, 1H), 3.75 (s, 3H), 2.90 (t, *J* = 7.2 Hz, 2H), 2.65 (t, *J* = 7.2 Hz, 2H) ppm; ^{13}C NMR ($CDCl_3$, 75 Hz) δ_C 172.9, 140.6, 139.7, 128.8, 128.7, 128.6, 126.6, 126.5, 87.0, 79.3, 73.1, 54.4, 34.8, 21.3 ppm; Ms *m/e* (relative intensity): 235 (M^+ - 59, 76.36), 217 (3.21), 202 (3.65), 157 (3.23), 144 (2.56), 129 (4.32), 105 (100.00), 91 (48.44); HRMS for $C_{17}H_{15}O$: 235.1085; found: 235.1104.

Methyl (+)-2-hydroxyl-2-phenyl-5-^{t}butyldimethylsilyloxyl-3-yn-pentyrate (4d):

$Zn(OTf)_2$ (0.2 eq.) as additive, (1*S*, 2*S*)-**1** as ligand: Isolated in 83 % yield and 91 % ee (the reaction scale: Alkyne **3c** is 1.5 mmol, the α-keto ester **2a** is 0.5 mmol) as determined by HPLC analysis (Chiralcel AD, hexane / *i*-PrOH = 8 / 2, 254 nm) t_r 7.85 (minor), 8.53 (major); $[\alpha]_D^{20}$ = +23.5 (*c*, 0.71, $CHCl_3$); IR (neat) 3495, 2957, 2931, 2859, 1741, 1452, 1257, 1146, 1095, 1067, 837, 780, 697 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ_H 7.60 (m, 2H),

7.29 (m, 3H), 4.39 (s, 2H), 4.18 (s, 1H), 3.70 (s, 3H), 0.85 (s, 9H), 0.06 (s, 6H) ppm; ^{13}C NMR ($CDCl_3$, 75 Hz) δ_C 172.5, 139.2, 128.9, 128.5, 126.5, 126.4, 85.4, 82.8, 72.9, 54.4, 52.0, 26.0, 18.5, -4.9 ppm; Ms *m/e* (relative intensity) 334 (M^+, 0.35), 318 (100.00), 276 (22.22), 246 (45.05), 217 (19.49), 189 (23.75), 171 (32.83), 115 (36.90), 75 (42.68); HRMS for $C_{17}H_{23}SiO_4$: 319.1354; found: 319.1360.

Methyl (+)-2-hydroxyl-2-[(*N*-^{t}butoxylcarbonyl)-3-indole]-4-phenyl-3-yn-butyrate (4e):

$Zn(OTf)_2$ (0.2 eq.) as additive, (1*S*, 2*S*)-**1** as ligand: Isolated in 81 % yield and 83 % ee (the reaction scale: Alkyne **3a** is 2.5 mmol, the α-keto ester **2c** is 0.5 mmol) as determined by HPLC analysis (Chiralcel AD, hexane / *i*-PrOH = 7 / 3, 254 nm) t_r 10.240 (minor), 14.593 (major); $[\alpha]_D^{20}$= +8.93 (*c*, 3.54, $CHCl_3$); IR (neat) 3474, 2928, 1739, 1453, 1373, 1255, 1156, 1080, 751, 691 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ_H 8.20 (d, *J* = 8.0 Hz, 1H), 7.95 (s, 1H), 7.80 (d, *J* = 7.5 Hz, 1H), 7.52 (m, 2H), 7.35 (m, 4H), 7.25 (m, 1H), 4.30 (br, 1H), 3.80 (s, 3H), 1.72 (s, 9H) ppm; ^{13}C NMR ($CDCl_3$, 75 Hz) δ_C 172.2, 149.7, 136.4, 132.2, 129.3, 128.6, 127.4, 125.7, 124.9, 123.2, 122.0, 120.7, 119.8, 115.6, 86.5, 86.0, 84.4, 69.3, 54.6, 28.4 ppm; Ms *m/e* (relative intensity) 389 (M^+-16, 1.21), 347 (21.99), 333 (13.26), 291 (100.00), 247 (63.27), 206 (16.48), 144 (17.05), 129 (55.79), 57 (68.39); HRMS for $C_{24}H_{23}NO_5$: 405.1562; found: 405.1569.

Methyl (+)-2-hydroxyl-2-[(*N*-^{t}butoxylcarbonyl)-3-indole]-6-phenyl-3-yn-hexyrate (4f):

$Zn(OTf)_2$ (0.2 eq.) as additive, (1*S*, 2*S*)-**1** as ligand: Isolated in 76 % yield and 86 % ee (the reaction scale: Alkyne **3b** is 2.5 mmol, the α-keto ester **2c** is 0.5 mmol) as determined by HPLC analysis (Chiralcel AD, hexane / *i*-PrOH = 75 / 25, 254 nm) t_r 13.71 (minor), 15.64 (major); $[\alpha]_D^{20}$= +14.4 (*c*, 1.265, $CHCl_3$); IR (neat) 3487, 2979, 2930, 2239, 1737, 1454, 1374, 1257, 1157, 1089, 1060, 1021, 749, 700 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ_H 8.15 (d, *J* = 8.1 Hz, 1H), 7.85 (s, 1H), 7.65 (d, *J* = 7.9 Hz, 1H), 7.35-7.20 (m, 7H), 4.05 (br, 1H), 3.80 (s, 3H), 2.90 (t, *J* = 7.6 Hz, 2H), 2.60 (t, *J* = 7.6 Hz, 2H), 1.65 (s, 9H) ppm; ^{13}C NMR

($CDCl_3$, 75 Hz) δ_C 172.4, 140.5, 128.7, 128.6, 128.2, 127.3, 126.6, 125.6, 124.8, 123.1, 120.6, 120.0, 115.5, 86.3, 84.3, 68.8, 54.4, 34.9, 29.9, 28.8, 21.3 ppm; Ms *m*/*e* (relative intensity) 375 (M^+ - 57, 14.01), 319 (67.32), 275 (33.99), 257 (9.86), 206 (22.32), 144 (26.39), 84 (42.56), 57 (100.00); HRMS for $C_{26}H_{27}NO_5$: 433.1889; found: 433.1889.

Methyl (+)-2-hydroxyl-2-[(N-^{t}butoxylcarbonyl)-3-indole]-5-^{t}butyldimethylsilyloxyl-3-yn-pentyrate (4g):

$Zn(OTf)_2$ (0.2 eq.) as additive, (1*S*, 2*S*)-**1** as ligand: Isolated in 67 % yield and 81 % ee (the reaction scale: Alkyne **3c** is 2.5 mmol, the α-keto ester **2c** is 0.5 mmol) as determined by HPLC analysis (Chiralcel AD, hexane / *i*-PrOH = 8 / 2, 254 nm) t_r 8.13 (minor); 9.20 (major); $[\alpha]_D^{20}$= +18.9 (*c*, 1.42, $CHCl_3$); IR (neat) 3487, 2931, 2858, 1739, 1454, 1374, 1257, 1234, 1158, 1091, 1061, 837, 780, 748, 667 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ_H 8.10 (d, *J* = 7.5 Hz, 1 H), 7.80 (s, 1 H), 7.60 (d, *J* = 7.5 Hz, 1 H), 7.30 - 7.20 (m, 2 H), 4.40 (s, 2 H), 4.05 (br, 1 H), 3.75 (s, 3 H), 1.60 (s, 9 H), 0.85 (s, 9 H), 0.08 (s, 6H) ppm; ^{13}C NMR ($CDCl_3$, 75 Hz) δ_C 171.8, 149.4, 136.1, 127.0, 125.4, 124.7, 122.9, 120.4, 119.2, 115.3, 84.5, 84.1, 81.9, 68.6, 54.2, 51.7, 29.7, 28.2, 25.8, -5.2 ppm; Ms *m*/*e* (relative intensity) 415 (M^+ - 58, 17.06), 359 (100.00), 329 (18.78), 315 (45.27), 299 (28.66), 269 (17.01), 198 (14.24), 154 (51.86), 57 (88.89); HRMS for $C_{25}H_{35}NSiO_6$: 473.2192; found: 473.2213.

Ethyl (-)-(*R*)-2-hydroxyl-2-methyl-4-phenyl-3-yn-butyrate (4h):

$Zn(OTf)_2$ (0.2 eq.) as additive: Isolated in 11 % yield and 92 %ee (the reaction scale: Alkyne **3a** is 1.5 mmol, the α-keto ester **2d** is 0.5 mmol) as determined by HPLC analysis (Chiralcel OD, *i*-PrOH / hexane = 97/3, 254 nm) t_r 20.647 (minor), 23.900 (major); $[\alpha]_D^{20}$= -15.3 (*c*, 0.38, $CHCl_3$); IR (neat) 3484, 2988, 2940, 2238, 1739, 1599, 1491, 1445, 1251, 1150, 1126, 1017, 758, 692 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ_H 7.5-7.45 (m, 2H), 7.35-7.25 (m, 3H), 4.35 (q, *J* = 7.3 Hz, 2H), 3.75 (br, 1H), 1.80 (s, 3H), 1.35 (t, *J* = 7.3 Hz, 3H) ppm; ^{13}C NMR ($CDCl_3$, 75 Hz) δ_c 173.0, 132.1, 128.9, 128.5, 122.2, 88.7, 84.1, 68.5, 63.2, 27.4, 14.3 ppm; Ms *m*/*e* (relative intensity) 218 (M^+, 1.88), 210 (60.25), 173 (9.06), 145

(100.00), 129 (15.32), 115 (4.77), 43 (38.15); Anal. Cald for $C_{13}H_{14}O_3$: C, 71.54%; H, 6.47%. Foumd: C, 71.63%; H, 6.49%.

Stereochemistry determination: In order to determine the absolute configuration, adduct 4h was then hydrogenated with Pd-C in the pressure of 4 atm hydrogen to afford α-hydroxyl ester **6.** Comparing the optical rotation of the synthesized **6** (-26, c = 0.26, $CHCl_3$) and the rotation data of ethyl (*S*)-2-hydroxy-2-methyl-4-phenyl-butyrate, which has been reported as +29.6 (c = 2.4, $CHCl_3$), the absolute stereochemistry of the tertiary asymmetric alcohol carbon in **4h** was assigned as *R* configuration.

(+)-2-hydroxyl-2-phenylethynyl-3,3-dimethyl-pentalactone (4i):

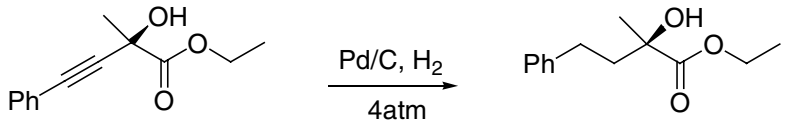
$Zn(OTf)_2$ (0.2 eq.) as additive, (1*S*, 2*S*)-**1** as ligand: Isolated in 95 % yield and 93.5 % ee (the reaction scale: Alkyne **3a** is 1.5 mmol, the α-keto ester **2e** is 0.5 mmol) as determined by HPLC analysis (Chiralcel AD, hexane / *i*-PrOH = 9 / 1, 254 nm) t_r 11.647 (major), 15.590 (minor); m.p. 66-70°C; $[\alpha]_D^{20}$= +8.89 (*c*, 3.92, $CHCl_3$); IR (neat) 3412, 2966, 2930, 2240, 1764, 1492, 1385, 1367, 1266, 1177, 1086, 1052, 1014, 997, 847, 757, 693 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ_H 7.65 (m, 2H), 7.55 (m, 3H), 4.35 (dd, J_1 = 25.4 Hz, J_2 = 8.7 Hz, 2H), 4.05 (br, 1H), 1.60 (s, 3H), 1.45 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$, 75 Hz) δ_C 174.9, 131.9, 129.2, 128.3, 121.2, 89.4, 82.8, 76.8, 74.7, 44.6, 20.5, 19.6 ppm; Ms *m/e* (relative intensity) 230 (M^+, 6.72), 202 (4.21), 186 (13.01), 175 (16.99), 171 (100.00), 157 (13.61), 143 (24.90), 129 (46.36), 115 (11.47); HRMS for $C_{14}H_{14}O_3$: 230.0941; found: 230.0942.

(-)-2-hydroxyl-2-(4-phenyl-1-butynyl)-3,3-dimethyl-pentalactone (4j):

$Zn(OTf)_2$ (0.2 eq.) as additive, (1*S*, 2*S*)-**1** as ligand: Isolated in 93 % yield and 94 % ee (the reaction scale: Alkyne **3b** is 1.5 mmol, the α-keto ester **2e** is 0.5 mmol) as determined by HPLC analysis (Chiralcel AD, hexane / *i*-PrOH = 95 / 5, 254 nm) t_r 22.21 (minor), 25.20 (major); $[\alpha]_D^{20}$= -17.5 (*c*, 0.45, $CHCl_3$); IR (neat) 3438, 2980, 2232, 1769, 1265, 1223, 1089, 1003, 697, 470 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ_H 7.30-7.15 (m, 5H), 3.95 (dd, J_1 =16.5 Hz, J_2 = 8.5 Hz, 2H), 3.20 (br, 1H), 2.79 (t, *J* = 7.3 Hz, 2H), 2.5 (t, *J* = 7.3 Hz, 2H), 1.05 (s, 3H), 1.04 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$, 75 Hz) δ_C 175.0, 140.0, 128.4, 126.5, 90.0, 76.6, 75.5, 74.3, 44.1, 34.3, 20.8, 20.3, 19.4 ppm; Ms *m/e* (relative intensity)

214 (M^+ - 44, 1.22), 199 (29.62), 181 (9.90), 157 (13.33), 129 (16.55), 91 (100.00), 69 (43.13); HRMS for $C_{16}H_{18}O_3$: 258.1246; found : 258.1251.

Ethyl (-)-2-hydroxyl-2-methyl-4-phenyl-butyrate (6):



4h **6**

A solution of **4h** (10 mg) in ethyl acetate (8 mL) was treated with 10% Palladium hydroxide on carbon (3 mg), and 4 atm of hydrogen in a Parr apparatus. After 24h, the reaction mixture was filtered through Celite and concentrated to obtain crude material, which was purified through flash chromatograph (petroleum: ethylacetate = 10:1) to afford colorless oil **6** (6 mg, 59%): $[\alpha]_D^{20}$= -26 (*c*, 0.26, $CHCl_3$); IR (neat) 3522, 3023, 2981, 2928, 2856, 1729, 1604, 1498, 1455, 1375, 1251, 1191, 1118, 1070, 1022, 749, 700 cm^{-1}; ^1H NMR ($CDCl_3$) δ_H 7.30 (m, 2H), 7.20 (m, 3H), 4.22 (q, *J* = 7.0 Hz, 2H), 3.35 (br, 1H), 2.80 (m, 1H), 2.45 (m, 1H), 2.05 (m, 2H), 1.45 (s, 3H), 1.30 (t, *J* = 7.0 Hz, 3H) ppm; ^{13}C NMR ($CDCl_3$, 75 Hz) δ_C 141.6, 128.4, 125.9, 74.1, 61.9, 41.7, 30.1, 26.3, 14.2 ppm; Ms *m/e* (relative intensity) 222 (M^+, 0.40), 205 (2.61), 183 (0.60), 149 (23.18), 131 (15.81), 118 (37.88), 105 (9.50), 91 (100.00), 43 (16.08); Anal. calcd. for $C_{13}H_{18}O_3$: C, 70.24%; H, 8.16%. found: C, 57.82%; H, 70.29%; N, 8.13%.